Biogenetic Relations involving the Neoflavanoids and their Congeners

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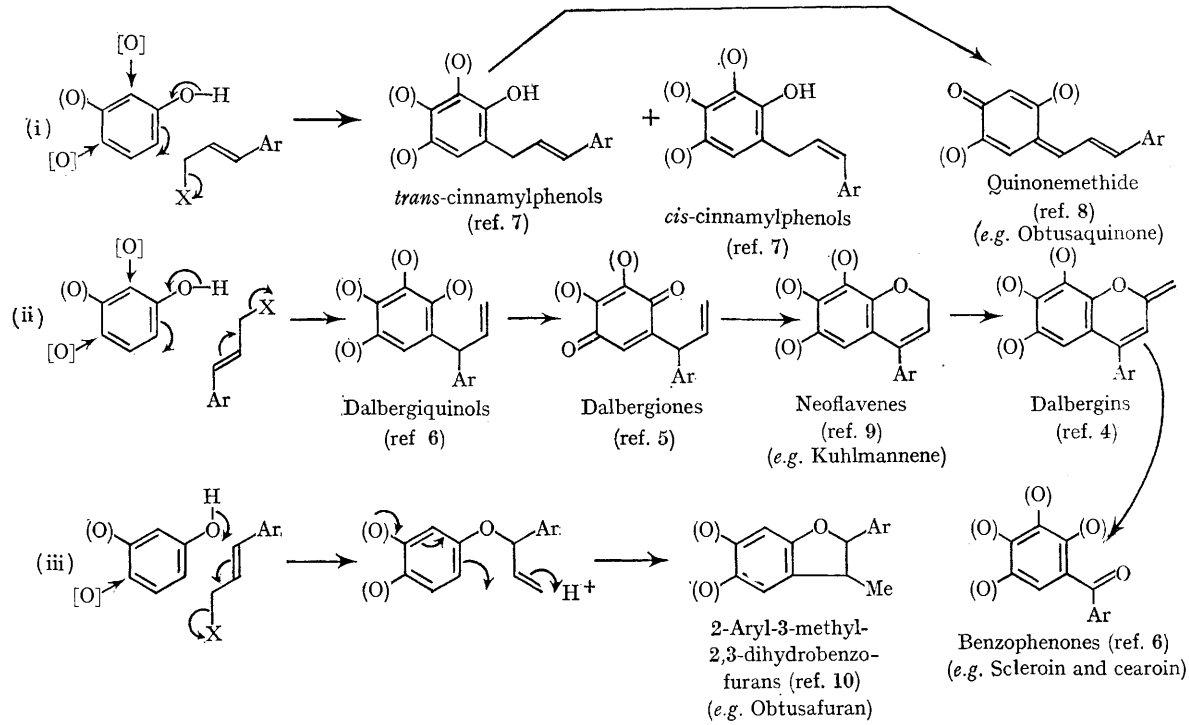
VARIOUS biogenetic theories have been put forward regarding the formation of neoflavanoids in plants, and it is now possible to consider these in relation to the results described in the preceding Communications. In the following discussion, the term phenolic unit (C_6) includes polyketide equivalents and the designation of the cinnamyl unit ($Ar{-}CH{=}CH{-}CH_2{-}X$) is general in that Ar can be oxygenated and X could be, for example, pyrophosphate. Proposals which have been made for neoflavanoid biosynthesis may be summarised as follows. (*a*) Two 1,2-aryl shifts from a chalcone precursor to give the neoflavanoid skeleton.[1–3] (*b*) β-Addition of a phenolic unit to a cinnamic acid, thus leading to the dalbergins (4-arylcoumarins) as progenitors of the neoflavanoid group.[4] This general process includes the so-called "Pechmann type condensation" of the phenolic unit with $Ar{-}CO{-}CH_2{-}CO_2H$.[1,2] (*c*) Alkylation of a phenolic unit by, for example, cinnamyl pyrophosphate or its equivalent.[3,5,6]

Pathway (*c*) (Scheme) is attractive in that it immediately accounts for the frequently observed natural co-occurrence of neoflavanoids and cinnamylphenols.[7] Thus cinnamylphenols could arise *directly* via route (i) and the observed occurrence[7] of natural *cis*- and *trans*-cinnamylphenols is mechanistically acceptable in terms of a *C*-cinnamylation process with S_N1-like characteristics. In relation to route (i), the newly discovered quinone methide, obtusaquinone,[8] may be regarded as a biotransformation product of a cinnamylphenol precursor. The neoflavanoids can be visualised [route (ii)] as a consequence of an allylic substitution process leading directly to the neoflavanoid skeleton of the dalbergiquinols which, by an appropriate oxidative sequence,[3,6] could provide the dalbergiones, neoflavenes[9] (*e.g.* kuhlmannene), dalbergins, and possibly some benzophenones (*e.g.* scleroin and cearoin) which are congeners[6] of the neoflavanoids. Route (iii) represents a further pathway from a phenolic C_6-unit and a cinnamyl C_9-precursor. This new proposal provides a satisfying route to the unusual 2-aryl-3-methyldihydrofurans[10] (*e.g.* obtusafuran).

It should be noted that routes (i), (ii), and (iii) are schematically represented as substitution reactions, but these are meant to be general representations which include other processes such as electrophilic substitution by cinnamyl cations. In the schemes the most frequently encountered oxygenated sites are indicated, and although cinnamylation *ortho* to phenolic groups is exemplified, the schemes cover processes initiated by *para*-cinnamylation as well (*e.g.* obtusastyrene).[7]

As the majority of the compounds isolated from *Dalbergia* and *Machaerium* species are heartwood constituents, our attempts to test these biogenetic proposals have not, as yet, been rewarding. The important results obtained by Kunesch and Polonsky[11] are at present compatible either with scheme (*b*) or with scheme (*c*), but the wide



SCHEME. *Biogenetic relations among the neoflavanoids and their congeners according to scheme* (c)

correlation of a large number of natural product constitutions which are phytochemically characteristic[3] of the botanically related *Dalbergia* and *Machaerium* genera, encourages us to favour the hypothetical pathways (i), (ii), and (iii) associated with scheme (*c*). These proposals represent a further biosynthetic function for the cinnamyl alcohols in addition to their established role in lignin biosynthesis[12] and the possible role[13] of cinnamyl phosphates as precursors of natural allyl phenols. The latter biogenetic proposal[13] is mechanistically equivalent to the nucleophilic attack by the phenol which is the first step in route (ii).

The latest biogenetic hypothesis for neoflavanoid biosynthesis proposed by Benn[14] involves, in our view, a sequence of reactions for which there are no reasonable mechanistic or laboratory analogies. Furthermore, this theory[14] does not allow for the extensive degree of structural correlation provided by our present biogenetic analysis (see Figure).

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